with supplementary information from study protocols, clinical study reports, and prescribing information. The trials were evaluated for any potential threats to study validity, such as selection bias, performance bias, and assessment bias, as well as the likelihood for chance effects instead of true effects. A detailed analysis of attrition (discontinuation or loss to follow up), which is a frequent issue in oncology studies, was also conducted to assess the presence of attrition bias. **RESULTS:** The integrated analysis and three pivotal trials were found to be of high-quality evidence and at low risk of bias and chance effects. Important quality features included a robust randomization process, high likelihood of patients remaining balanced and blinded throughout the study, as well as a high degree of adherence to assigned treatments. These and other factors, such as balance in co-interventions and in rates and reasons for discontinuation, make bias from attrition unlikely. **CONCLUSIONS:** The critical appraisal confirmed that the results of the integrated analysis and three pivotal trials were robust, with denosumab providing clinically meaningful benefit in patients with bone metastases from advanced cancer.

PCN20

IS METFORMIN EXPOSURE ASSOCIATED WITH IMPROVED SURVIVAL IN HEAD AND NECK CANCER PATIENTS? A LARGE POPULATION-BASED COHORT STUDY

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OBJECTIVES: Clinical studies of metformin in certain cancer types have demonstrated decreases in incidence and improvements in therapeutic response. Preclinical evidence supports multiple potential molecular pathways through which metformin may impart beneficial effects which impede the development and growth of head and neck cancer (HNC). We investigated the impact of metformin exposure following a diagnosis of HNC on the risk of all-cause mortality in a population-based cohort of Italian patients. **METHODS:** We used the Italian Emilia-Romagna Regional (RER) longitudinal healthcare database to conduct a retrospective cohort study following approximately 4 million adults (>=18) from 2003 to 2011. The RER database captures de-identified, fully-linkable demographic, hospital discharge including ICD-9 diagnostic and procedure codes, outpatient pharmacy, and specialty data for all residents of the region. Resection status and metastases were used to stage the HNC patients based on surgical procedures and secondary malignancies. Cox proportional hazard methods were used to model the covariate-adjusted time-dependent medication exposure survival association to minimize potential immortal-time-bias. **RESULTS:** During the study period, we identified 7,872 patients diagnosed with HNC after which 708 (8.99%) were exposed at some point to metformin and 3,626 (46.1%) died during follow-up (median = 2.98 years). Among them, after adjusting for potential confounders, we found no significant association between exposure to metformin and reduced risk of all-cause mortality (HR=1.03, 95% CI: 0.84 – 1.26). **CONCLUSIONS:** Our large population-based cohort study failed to find an advantage in survival outcomes for HNC cancer patients exposed to metformin, despite in-vitro mechanistic viability. Further research will be critical in clearly defining the role of metformin in HNC cancer survival using similar modeling approaches.

PCN21

IDENTIFICATION AND CHARACTERIZATION OF LONG TERM SURVIVAL POPULATION IN NON-SMALL-CELL LUNG CANCER PATIENTS TREATED WITH IMMUNOTHERAPIES

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OBJECTIVES: The aim of the study was to identify and characterize long term survival population of advanced non–small-cell lung cancer patients treated with immunotherapy. **METHODS:** Data from 717 patients coming from two expanded used program and from two randomized trials evaluating the efficacy of CIMAvaxEGF and Vaxira in patients with advanced NSCLC, were used. Mixture models were fitted to Overall Survival with one or two population components. All analyzes were made using the NLMIXED procedure in SAS. We used the diagnostic tools provided by this procedure to check the models' good of fit properties. The characterization of the two populations based in prognostic factors was done by classification tree models using RPART package in R. **RESULTS:** Two months of overall survival (OS) benefit were showed for CIMAvaxEGF and for Vaxira. The optimal mixture model with the fewest number of parameters that adequately describes the time survival data is a mixture model with 2 component distributions. Components represent short-term and long-term survival subpopulations. The proportions of the long term population increase with immunotherapy in 22% of patients for Vaxira and 18% for CIMAvaxEGF. The OS benefit was different for both subpopulation for both vaccines (vaxira: 2.08 months and 8.7 of OS benefit for short- and long- term survival populations respectively; CIMAvaxEGF: 1.96 months and 14.36 months of OS benefit for short- and long- term survival populations respectively). The performance status and the age were essential in the classification of the two populations. **CONCLUSIONS:** The results confirm that there are two subgroups among NLCLC patients. The separate analysis of subgroups can give more power to the evaluation of clinical trials. The use of mixture models in the analysis has implications for the design of new clinical trials. The use of classification trees allowed a good characterization of the two populations.

PCN22

PRALATREXATE TREATMENT IN PATIENTS WITH RELAPSED OR REFRACTORY PERIPHERAL T-CELL LYMPHOMA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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OBJECTIVES: Pralatrexate, the first drug to gain US FDA approval for treatment of relapsed/refractory peripheral T-cell lymphomas (PTCL) in 2009, was aimed to treat PTCL-not otherwise specified, angioimmunoblastic T-cell lymphoma, adult T-cell leukemia/lymphoma, and anaplastic large cell lymphoma patients. There was absence of consensus regarding standard therapeutic measures. Randomized controlled trials comparing different treatment approaches for PTCL are very limited due to its rarity and the heterogeneity of subtypes. **METHODS:** We attempt to collect clinical approved evidences for the efficacy and safety of pralatrexate as a salvage treatment for relapsed/refractory PTCL by systematic review. Searches based on According to National Comprehensive Cancer Network (NCCN) Guidelines and explicit inclusion criteria and exclusion criteria are set for literature searching in PubMed, Cochrane Library and Web of Science. We evaluate primary efficacy outcome (ORR and 95% CI), secondary efficacy outcomes (overall survival and progression-free survival duration) and safety outcomes. **RESULTS:** Twenty-four studies were initially identified for abstract screening. After further checking by two independent reviewers, 11 records eligible for full-text reviews. A total of 351 relapsed/refractory PTCL patients were investigated from 11 studies. The median age for those treated with pralatrexate were ranged from 45 to 61.5. Before ORRs were compared, we adjusted the severity of diseases due to heterogeneous distribution of PTCL subtypes. **CONCLUSIONS:** Our study results indicate that pralatrexate is the salvage treatment of choice for the heavily pretreated patients.

PCN23

HETEROGENEITY OF TREATMENT EFFECT OF ANDROGEN DEPRIVATION THERAPY IN PATIENTS WITH INCIDENT METASTATIC PROSTATE CANCER

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OBJECTIVES: In the era of personalized medicine, oncologists seek to tailor treatments for their patients based on indicators of differential response to treatment. The objective of this study was to estimate the survival benefit associated with androgen deprivation therapy (ADT) receipt in elderly Medicare patients newly diagnosed with Stage 4 metastatic (S4M1) prostate cancer across patient subgroups defined by Gleason score and age. **METHODS:** We analyzed elderly men diagnosed with S4M1 prostate cancer between 2004-2009 in the SEER-Medicare datasets and followed through 2010 or until loss to follow-up. An inverse probability weighted Cox proportional hazards model with ADT-by-age and ADT-by-Gleason score interaction terms was used to estimate overall survival (OS) and prostate cancer-specific survival (PCSS). **RESULTS:** Among 4,691 patients, 3,426 (73%) men received ADT within the first 6 months of diagnosis and 1,265 (27%) men did not receive any form of ADT (median follow-up: 17 months). There were 3,173 total deaths in the cohort, 1,923 (61%) deaths of which were due to prostate cancer. Compared to the non-ADT group, ADT users had a 52%, 39%, 59%, and 62% relative reduction in the risk of all-cause death in men aged 66-70, 71-75, 76-80, and 80+, respectively (statistically significant; based on stratified hazard ratios from the Cox model). A similar trend was observed for PCSS for the age subgroups. Compared to the non-ADT group, ADT users had a 54% and 57% relative reduction in the risk of all-cause deaths and prostate cancer-specific deaths in men with Gleason 8-10, respectively. However, the startified hazard ratios for Gleason <8 showed no OS benefit (Gleason 2-6: [1.4 (0.79-2.44)] and Gleason 7: [0.88 (0.68-1.14)] or PCSS benefit (Gleason 2-6: [1.09 (0.53-2.20)]; Gleason 7: [1.05 (0.72-1.51)]. **CONCLUSIONS:** ADT was beneficial in terms of OS and PCSS for all age and Gleason score subgroups except men with Gleason score 2-6 and 7.

PCN24

NUCLEOSIDE ANALOGUES, STATINS AND THE RISK OF HEPATOCELLULAR CARCINOMA IN PATIENTS WITH HEPATITIS B VIRUS INFECTION

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OBJECTIVES: Statins may have protective effects against hepatocellular cancer, but no studies have focused on their clinical interactions with nucleoside analogues(NAs) in patients with chronic hepatitis B virus (HBV) infection. The purpose of this study was to investigate the association between the use of NAs, statins and the risk of hepatocellular carcinoma (HCC) in HBV-infected patients. **METHODS:** A population-based matched cohort study of 91,265 HBV-infected patients enrolled in the Taiwan National Health Insurance Research Database since October, 2003 and December, 2010. 18,253 patients with NAs use were 1:4 matched as 73,012 patients without NAs use according to index date, age, sex, diabetes, liver cirrhosis, hypertension, hyperlipidemia, biliary tract stones, chronic renal injury, alcohol related diseases, and COPD. Cox proportional hazards regression model for drug exposures was employed to evaluate the association between NAs, statin use and HCC risk. **RESULTS:** 2841 patients were diagnosed with HCC during 262489.6 person-years; the overall incidence rate was 1082.3 cases per 100,000 person-years or 1% per year. The mean follow-up time was 2.9 years. We observed a significantly lower risk of HCC among NAs users than among non-users (adjusted HR, 0.42; 95%CI, 0.37-0.48) after controlling for potential confounders, which was also found in statin users. In addition, we found there was a synergistic effect on NAs and statins uses. The adjusted HRs were 0.27 (95%CI, 0.12–0.59), 0.42 (95%CI, 0.37–0.48), and 0.62 (95%CI, 0.47–0.84) for patients with both NAs, statin user, only NAs user, only statin user when comparing with non-users. **CONCLUSIONS:** NAs are effective in suppressing HBV replication and in ameliorating HBV related liver disease. Statins may have protective effects against hepatocellular cancer, and our study found there was a synergistic effect on HCC risk reduction of NAs and statins use.

PCN25

INCIDENCE AND PREVALENCE OF BASAL CELL CARCINOMA IN A LARGE UNITED STATES COMMERCIALLY INSURED POPULATION

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